Claims 1-8 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) has possession of the claimed invention at the time that the application was filed.

The Examiner asserts that the amendment to claim 1, deleting "single stranded" from "collecting the hybridized single stranded nucleic acids" appears to be new matter because the description at the bottom of page 17 would be interpreted by one of skill in the art as collecting single stranded nucleic acids such as after a denaturing step.

Applicant believes that this confusion arises from translational errors in the original claim 1 and the corresponding description. With this amendment, Applicants has amended claim 1 and corrected the specification at page 3, lines 5-9; page 17, lines 6-11 and page 17, second line from the bottom to correct these translational errors. Support for these amendments is found in the present specification at page 20, lines 5-10; page 20, fifth line from the bottom to page 21, line 1; page 25, last line to page 26, line 2; and page 30, lines 10-14. As can be seen from this description, the single stranded nucleic acid may be collected as the hybridized nucleic acids with its complementary nucleic acid. That is, the hybridized nucleic acids may be collected.

Support for the present amendment is also found in Applicant's priority document and a verified translation will be provided to the Examiner upon request.

The Examiner also states that the description of the substrate at pages 4-5 does not present a clear picture of how rubbing off a portion of the substrate with covalently attached nucleic acids may be accomplished.

In response, the fact that rubbing off enables collection of nucleic acids is evidenced by Examples 1 (6)-(7), 2 (6)-(7), 3 (5), and 4 (2) of the present specification.

Applicant explains the mechanism of rubbing off as follows. When the immobilized portion is rubbed off with, for example, a pipette tip or the like, the immobilized hybridized nucleic acid (including hybridized single-stranded nucleic acid) is physically separated at the portion binding to the substrate. If the substrate is not flaky or fragile, the substrate itself is not separated and only the hybridized nucleic acid is separated by cutting or tearing of the nucleic acid. If the substrate is flaky or fragile or has a flaky fragile layer thereon, the surface of the substrate may be physically destroyed and therefore the hybridized nucleic acid may be collected with the surface portion of the substrate. See a schematic drawing attached as Appendix.

In view of the above, reconsideration and withdrawal of all grounds of rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that the method steps are *non sequitur* to the preamble in that they do not result in separating nucleic acids as recited therein. In response, Applicant has modified the preamble to delete "separating and" as suggested by the Examiner.

The rejection based upon claim 2 has been obviated by amendment. Support for the amendment is found in the present specification at page 10, lines 14-21.

In view of Applicant's amendments, withdrawal of this ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1 and 3-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cantor et al. in view of general teaching in the art as exemplified by Rothberg et al. and Alam.

The Examiner asserts that Cantor et al. disclose a method similar to that of the claimed invention set forth in claim 1 wherein a sample nucleic acid solution is contacted with a nucleic acid immobilized substrate which provides immobilized portions of single stranded nucleic acids such that single stranded nucleic acids contained in the sample hybridize with the immobilized nucleic acids followed by collecting the hybridized nucleic acids by denaturing elution. While the Examiner acknowledges that Cantor et al. differ from the claimed invention by not disclosing a collection method, the Examiner asserts that the phenomena of transfer of solutes by contact between wet and dry surfaces and between wet surfaces was well known and that Cantor et al. teach the transfer of nucleic acids from a master array to a substrate by simply touching plastic coated pins carrying nucleic acids in solution to a surface., that Rothberg et al. teach the use of manual and robotic means to transfer nucleic acid probes to a glass surface and Alam describes a method for electroeluting nucleic acids from gels wherein nucleic acids are recovered with a pipet tip.

In response, collection of hybridized nucleic acids by rubbing off or shaving off immobilized portions is neither taught nor suggested by any of the cited references.

Cantor et al. describe that a master array consisting of a set of pins, each of which contains immobilized biotinylated DNA strands, is touched to a streptavidin-coated surface of a replica, held at a temperature above the Tm of the complexes on the master array (col. 21, lines 32-45). No rubbing nor shaving of a substrate with the pins is taught or suggested.

Rothberg et al. describe that a probe solution is transferred to a slide by touching the surface of the slide either with blunt-ended needle tips or with pipette tips that had been dipped in the appropriate solution of the appropriate probes (col. 82, lines 60-64). Neither rubbing nor shaving of a substrate is taught or suggested.

Alam describes that after electroelution, a solution of the biomolecules accumulated against the membrane is sucked up using a pipette tip (col. 6, lines 41-42 and 60-66). Rubbing or shaving of a substrate with the tip is neither taught nor suggested.

As is well-known, a *prima facie* case of obviousness requires that three basic criteria be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed invention and the reasonable expectation of success must both be found in the prior art, and must not be based on Applicants' disclosure. In this case, the references cited fail to teach or suggest all of the claim limitations.

In view of Applicant's arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

Claims 2-4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cantor et al. as applied to claims 1 and 3-8 above in view of Takenishi et al.

Takenishi et al is cited for their teaching of a plate carrying a carbodiimide. However, Takenishi et al. are silent about means of rubbing off and shaving off the immobilized portions to collect the immobilized nucleic acids. Consequently, Takenishi et al. cannot correct the deficiency of the Cantor et al. reference discussed above.

In view of Applicant's arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: March 7, 2003

By: Che S. Chereskin

Che Swyden Chereskin
Registration No. 41,466
Agent of Record
Customer No. 20,995

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 2, line 22 has been amended as follows:

That is, the present invention provides the ~~followings~~following.

(1) A method for ~~separating and~~ collecting nucleic acids, which comprises:

a step of bringing a sample nucleic acid solution into contact with a nucleic acid-immobilized substrate comprising a substrate and two or more kinds of single-stranded nucleic acids separately immobilized on the substrate, to allow hybridization of the immobilized single-stranded nucleic acids and single-stranded nucleic acids complementary to the immobilized single-stranded nucleic acids, and

a step of ~~separating~~ collecting each of the hybridized single-stranded nucleic acids separately according to immobilized portions of the immobilized nucleic acids, ~~to collect the hybridized single-stranded nucleic acids~~ without disassembling the nucleic acid-immobilized substrate.

(2) The method according to (1), wherein the nucleic acid-immobilized substrate is a substrate carrying a compound having a carbodiimide group.

(3) The method according to (1) or (2), wherein the nucleic acid-immobilized substrate is a DNA microarray.

(4) The method according to any one of (1) to (3), wherein the substrate has a plate-like shape.

The paragraph beginning at page 16, second line from the bottom has been amended as follows:

The method for ~~separating and~~ collecting nucleic acid of the present invention comprises a step of bringing a sample nucleic acid solution into contact with the aforementioned nucleic acid-immobilized substrate to allow hybridization of two or more kinds of the single-stranded nucleic acids carried by the nucleic acid-immobilized substrate and single-stranded nucleic acids complementary thereto, and a step of ~~separating~~ collecting the hybridized single-stranded nucleic acids separately according to immobilized portions of the immobilized nucleic acid, ~~to collect the hybridized single-stranded nucleic acids~~ without disassembling the nucleic acid-immobilized substrate.

The paragraph beginning at page 17, line 25 has been amended as follows:

As the method for collecting hybridized single-stranded nucleic acids, various known methods can be used so long as each of the hybridized single-stranded nucleic acids can be ~~separated and collected~~separately collected according to immobilized portions of the immobilized nucleic acids without disassembling the nucleic acid immobilized substrate. For example, the following methods can be used.

1. Rubbing off only a portion on which the nucleic acids are immobilized, of the nucleic acid-immobilized substrate with a tip of micropipette or the like after the hybridization.

2. Shaving off a portion (dot) on which nucleic acids are immobilized together with a portion of the substrate by using a spotter having a pinpoint deformed into a shovel shape.

3. Filling a pin of a spotter or a capillary pipet with a DNA-denaturing agent such as an alkali solution, and bringing a tip of the pin or the capillary pipet into contact with dots on the nucleic acid-immobilized substrate in which nucleic acids desired to be collected are hybridized to denature the nucleic acids and transfer the nucleic acids into the pin or the capillary pipet. The nucleic acids can be collected by immersing the pin or the capillary pipet into another solution, or physically transferring the nucleic acids in the pin or the capillary pipet into another container.

IN THE CLAIMS:

Claims 1 and 2 have been amended as shown.

Claim 1. (Three times amended) A method for ~~separating and~~ collecting nucleic acids, which comprises:

contacting a sample nucleic acid solution with a nucleic acid-immobilized substrate comprising a substrate and single-stranded nucleic acids having different nucleotide sequences, said single-stranded nucleic acids being each separately immobilized on the substrate, whereby immobilized portions of the immobilized single-stranded nucleic acids are provided on the nucleic acid-immobilized substrate;

hybridizing the immobilized single-stranded nucleic acids and single-stranded nucleic acids contained in the sample nucleic acid solution and complementary to the immobilized single-stranded nucleic acids to form hybridized nucleic acids; and

collecting the hybridized nucleic acids separately according to the immobilized portions by a means selected from the group consisting of:

(1) rubbing off the immobilized portions; and

(2) shaving off the immobilized portions.

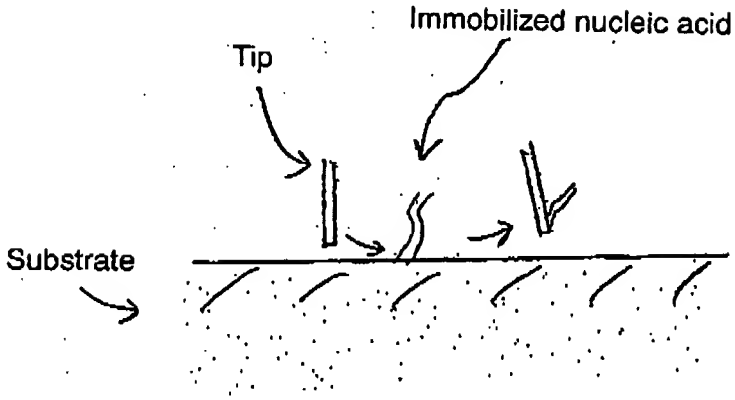
Claim 2. (Amended) The method according to claim 1, wherein the nucleic acid-immobilized substrate is ~~a substrate carrying a compound having a carbodiimide group~~a substrate on which the single-stranded nucleic acids having different nucleotide sequences are immobilized via a compound having a carbodiimide group carried on the substrate.

AMEND
H:\DOCS\CSC\CSC-4625.DOC
030703

APPENDIX

Appendix

When the substrate is not flaky or fragile



When the substrate is flaky or fragile